

### REMARKS

#### **Claim amendments**

Applicant amends the claims to recite the process by which probability curves of the type shown in FIGS. 15B-15C are represented as continuous grade output. Support for the amendment can be found in the discussion of FIGS. 12A through 15C on pages 21-23 of the specification.

Applicant seeks to distinguish between lipid-rich atheromas, and all other tissue. These two types of tissue have different NIR spectra, which ultimately yield different chemometric prediction scores. Thus, the chemometric prediction score provides a way to discriminate between these two classes. If this score is in excess of some threshold, the tissue is classified as a lipid-rich atheroma. Otherwise, it is not.

A difficulty that arises is that it is not all that easy to determine an appropriate value of the threshold. This occurs both because the threshold would differ from one individual to the next, and because the classification problem is inherently probabilistic.

For example, in some individuals, a particular chemometric prediction score may be highly indicative of lipid-rich atheroma. Whereas in another individual, the exact same score may be more indicative of other kinds of tissue. This is shown in FIG. 14 for three different patients.

In addition, lipid-rich atheromas may yield different scores with different probabilities. This results in probability distributions as shown in FIG. 15A. There also exists a probability distribution for other types of tissue. Unfortunately, these two probability distributions tend to overlap, as shown in FIG. 15A.

The consequence of this overlap are twofold: First, for any threshold value one selects, there will exist a probability of false alarm, which occurs when normal tissue is misclassified as

lipid-rich atheroma. Second, for any threshold value one selects, there exists a probability of leakage, which occurs when a lipid-rich atheroma is misclassified as normal tissue. The particular threshold chosen thus controls the false alarm rate and the leakage rate.

In most clinical settings, one would like to choose a threshold that achieves a particular compromise between false-alarm rate and leakage rate. However, the choice of the threshold will in general depend on the shapes of the two probability distributions. These in turn will change from one patient to the next.

It is clear that the most likely mistakes will be made within a band of scores at which the two distributions shown in FIG. 15A have comparable values. The width of this band will, again, change from one patient to the next. As a result, it is useful to define the location and width of this band in response to the unique characteristics of a patient.

Amended claim 59 recites a way to control the location and width of the band to provide greater flexibility to someone attempting to detect lipid-rich atheroma in a patient.

#### *Fantini*

In the preceding office action, the Examiner regarded *Fantini* as teaching "converting the set of numbers into a continuous grade output that characterizes the tissue without a threshold." It is therefore appropriate to discuss *Fantini* in some detail in view of the amendment to claim 59.

*Fantini* teaches creating an image of breast tissue. At each point in the tissue, *Fantini* assigns a value that depends on properties of the tissue at that point. This value is then translated into a gray-scale value and used in rendering an image of the breast tissue. As it turns out, certain gray-scale values are correlated with cancerous tissue. Thus *Fantini* provides a way to visually identify cancerous tissue.

According to *Fantini*, the prior art method of displaying an image that highlights cancerous tissue is one that defines a function  $N(x, y)$  whose value at a point  $(x, y)$  corresponds to

a product of tissue thickness and the intensity of transmitted light at that point.<sup>1</sup> FIG. 3 shows an image of breast tissue using this  $N(x, y)$ .

*Fantini* improved upon the prior method by instead defining a function that depends on second derivatives of  $N(x, y)$ . In particular, at each point  $(x, y)$ , *Fantini* evaluates four partial derivatives, each corresponding to a different direction.<sup>2</sup> The resulting image, shown in FIG. 5, shows much greater resolution than the prior art image in FIG. 3.

#### **Difference between *Fantini* and claimed invention**

*Fantini* does not recognize variation between individuals. Nor does *Fantini* recognize any possibility that cancerous tissue might take certain values of  $N$  or  $N''$  with certain probabilities. There is no way, in *Fantini*, to change the way cancerous tissue is displayed in response to differences between individuals. Nor is there any way to control leakage and false-alarm rates.

As amended, claim 59 recites processing spectral data to generate a set of numbers, with each of those numbers being "indicative of a probability that a portion of selected tissue belongs to a particular class."

In *Fantini*, the "set of numbers" would most likely correspond to the values of either  $N(x, y)$  or  $N''(x, y)$ . With that being the case, the claim limitation is clearly not met.

The manner in which both  $N$  and  $N''$  is calculated is clearly shown in paragraphs 57 and 58. It is quite plain that all one needs to know to calculate either  $N(x, y)$  or  $N''(x, y)$  is  $r(x, y)$ , which is the breast thickness, and  $ac(x, y)$ , which is a measure of the way light interacts with the breast tissue at  $(x, y)$ . There is nothing probabilistic about breast thickness. It is simply something one measures. Nor is there anything probabilistic about transmission of light, which again is something one simply measures. It is thus clear that there is nothing at all probabilistic about  $N$  or  $N''$ . Both of these functions are purely deterministic quantities that depend on measured physical parameters.

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<sup>1</sup> *Fantini*, paragraph 57.

<sup>2</sup> *Fantini*, paragraph 58.

Fundamentally, the *Fantini* problem is a classification problem much like that which Applicant has addressed. In *Fantini*, there could be a probability distribution for both cancerous and non-cancerous tissue, and if so, there would be issues of false alarm rates and leakage rates that would accompany a choice of threshold for distinguishing between these two probabilities.

However, *Fantini* does not mention any of this. *Fantini* simply calculates  $N^*(x,y)$ , creates a map of the breast, and uses a gray-scale to show values of  $N^*(x,y)$ . Issues relating to probability distributions, false alarm rates, leakage rates, choices of thresholds, possible variations between individuals, all of which Applicant was concerned with, are completely absent from *Fantini*.

#### Summary


Now pending in this application are claims 59 to 69, of which claim 59 is independent.

Enclosed is a petition for extension of time with authorization to charge the extension fee. No additional fees are believed to be due in connection with the filing of this response. However, to the extent fees are due, or if a refund is forthcoming, please adjust our deposit account 06-1050, referencing attorney docket "12258-030001."

Respectfully submitted,

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